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Short-and medium-term associations of particle number concentration with cardiovascular markers in a Puerto Rican cohort

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ABSTRACT

Air pollution has been linked to adverse cardiovascular outcomes; however, susceptibility may vary by population. Puerto Rican adults living in the US may be a susceptible group due to a high rate of adverse cardiovascular events. We evaluated the effect of changes in ambient particle number concentration (PNC, a measure of ultrafine particles) and effects on biomarkers of cardiovascular risk in the Boston Puerto Rican Health Study (BPRHS), a longitudinal cohort (n = 1499). Ambient PNC was measured at a fixed site between 2004 and 2013 and daily mean concentrations were used to construct PNC metrics, including lags of 0, 1 and 2 days and moving averages (MAs) of 3, 7 and 28 days. We examined the association of each metric with C-reactive protein (CRP) and blood pressure. Each model included subject-specific random intercepts to account for multiple measurements. An interquartile range (IQR) increase in PNC was associated with CRP for all metrics, notably a 3-day increase in PNC was associated with a 7.1% (95% CI: 2.0%, 12.2%) increase in CRP. Significant associations with CRP were seen in women, but not men; with current and former (but not non-) smokers; participants younger (but not older) than 65 y; those without diabetes (but not with), and those with (but not without), hypertension. Our study extends knowledge about the health effects of air pollution to a vulnerable population that has been understudied.

1. Introduction

Particulate matter pollution in ambient air is a significant contributor to the global burden of disease (Lim et al., 2012). A large proportion of this burden is the association between airborne particulate matter and cardiovascular morbidity and mortality (Brook et al., 2010). Multiple mechanisms may explain these associations, including pulmonary inflammation leading to the release of inflammatory cytokines and acute-phase proteins, resulting in endothelial dysfunction, atherosclerosis, plaque rupture and thrombosis (Brook et al., 2010; Knol et al., 2009). C-reactive protein (CRP) is an acute-phase protein and a marker of systemic inflammation from cellular injury that has been studied as a subclinical indicator of this mechanistic pathway (Brook et al., 2010; Li et al., 2012). Particulate matter has been associated with increased CRP in short timeframes in studies of various cohorts including the young, elderly and those with co-morbid conditions (Brook et al., 2010). A second mechanism for the biological effects of PM involves disruption of the autonomic nervous system, vasoconstriction and heart function abnormalities (Brook et al., 2010; Knol et al., 2009). Supporting evidence includes associations between particulate matter and blood pressure, which is a traditional predictor of future adverse cardiac events. (Brook et al., 2010; Giorgini et al., 2016).

While many studies have examined cardiovascular effects of particulate matter less than 2.5 µm in diameter ($PM_{2.5}$), there is evidence of potentially greater impacts from smaller particles including those that are classified as ultrafine particles (UFP, aerodynamic diameter < 0.1 µm) (Knol et al., 2009). Total particle number concentration (PNC) in urban areas is dominated by UFP, and many studies have determined

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that PNC is a reliable proxy for UFP (Kumar et al., 2014; Morawska et al., 1998; Pant and Harrison, 2013). We use the terms PNC or UFP as appropriate in this paper, depending upon the specific measurements made in particular studies, as well as refer to them jointly as PNC/UFP.

We have identified several studies that evaluated short-term associations of CRP with PNC/UFP (Delfino et al., 2009; Fuller et al., 2015; Hertel et al., 2010; Karottki et al., 2015; Wang et al., 2016). The majority identified non-significant increases in CRP with higher UFP up to 28 days prior. A recent review of studies of short-term ambient UFP and blood pressure reported mixed results for associations with systolic blood pressure (SBP) and diastolic blood pressure (DBP) (Magalhaes et al., 2018). Several studies reported higher effect estimates linking UFP and blood pressure, but only a few reached statistical significance. A small number reported an inverse association between UFP and DBP (Magalhaes et al., 2018). It is important to note that the review did not include any studies that examined UFP for more than 7 days.

Another key question to explore is whether populations with pre-existing burdens of chronic disease may be especially susceptible to UFP exposures. Cardiovascular disease patients in New York State were found to experience higher associations between UFP and CRP and blood pressure (Rich et al., 2012). In a German cohort, patients with type 2 diabetes or impaired glucose tolerance with specific genotypes showed a greater response in CRP and inflammatory markers with exposure to PNC, compared to those without these conditions (Rückerl et al., 2014).

Puerto Ricans may be susceptible to air pollution due to a high prevalence of chronic diseases. Puerto Ricans make up the second largest Hispanic subgroup in the U.S., after Mexican Americans, and are at increased cardiovascular risk compared to the American population at-large, as well as other Hispanic groups (Tucker et al., 2010). Puerto Rican women had the highest prevalence of metabolic syndrome in the Hispanic Community Health Study/Study of Latinos (HCHS/SOL) (Heiss et al., 2014). In the Multi-ethnic Study of Atherosclerosis (MESA), Puerto Ricans had the highest measures of left ventricular mass index (LVMI) and ankle-brachial pressure index (ABI) (Allison et al., 2008). As higher cardiovascular risk may confer susceptibility to air pollution, it is important to evaluate among this population.

In the present study, we explore air pollution and cardiovascular health using data from the Boston Puerto Rican Health Study (BPRHS); a longitudinal cohort study of Puerto Rican adults designed to examine physical and social predictors of cardiovascular health (Tucker et al., 2010). In particular, the BPRHS was designed to gather data on behaviors and exposures, including environmental particulate matter, that may explain health disparities between Puerto Ricans, other Hispanic groups and non-Hispanic whites. The cohort was recruited from the Boston metropolitan area beginning in 2004. The rich and detailed information available include cardiovascular health indicators and several other risk factors. The purpose of this paper is to evaluate the association between changes in short-term ambient PNC and cardiovascular function markers. Specifically, we evaluate the impact of selected lags and moving averages on CRP and blood pressure. In addition, this is the first analysis, to our knowledge, that examines the impact of ambient PNC for up to 28 days on blood pressure (Magalhaes et al., 2018).

2. Materials and methods

2.1. Study design and population

The methods for recruitment and data collection are detailed elsewhere (Tucker et al., 2010) and presented briefly here. Participants were recruited from the Boston metropolitan area (primarily the cities of Boston, Chelsea and Lawrence) and were between the ages of 45 and 75 years at enrollment. Recruitment was conducted via door-to-door solicitation in census tracts identified in the 2000 Census as having 25 or more Puerto Rican adults. In addition, participants were identified through referrals, calls to the study office, and community events. Participants were enrolled in the study on an ongoing basis from 2004 to 2009 (baseline). Based on entry into the study, follow up took place after approximately 2 years (2006–2011) and after approximately 5 years (2011–2015). Baseline questionnaires and clinical measurements were completed in English or Spanish at the participant's home by trained bilingual staff. Demographic information on age, household income, education, employment history and family structure were collected at the baseline visit. Data on health outcomes and measures were taken at baseline and at the year 2 and 5 follow up visits. The study was approved by the Institutional Review Boards at Tufts Medical Center, Northeastern University and University of Massachusetts-Lowell. All participants provided written informed consent.

2.2. Biomarker measurement

We utilized data on CRP, systolic and diastolic blood pressure. These measurements were made at baseline and at up to two subsequent visits, resulting in repeated measures for the majority of participants (Tucker et al., 2010). Blood pressure measurements were taken while the participant was seated quietly, using an electronic sphygmomanometer (DinamapTM Model 8260, Critikon, Tampa, FL). SBP and DBP were measured three times during each visit and the second and third measurements were averaged. Standing height, weight, waist and hip circumference were measured in duplicate for the calculation of body mass index (BMI) and waist-hip ratio. A certified phlebotomist drew venous blood samples from each participant, in the home. CRP was analyzed in blood serum using the Immulite 1000 High Sensitive CRP Kit (LKCRP1) on the Immulite 1000 (Seimens Medical Solutions Diagnostics, Los Angeles, CA).

2.3. Air pollution measurement

We characterized ambient PNC using a fixed monitor located within 10.5 km of all participants. The monitor was positioned on a rooftop (six floors above street level) at the Countway Library of Medicine of Harvard Medical School on Huntington Avenue in Boston. Measurements at this site have been found to be a good estimate of temporal variation in PNC at other locations in Boston (Fuller et al., 2012). In addition, PNC at this height has been shown to be representative of ground level concentrations (Wu et al., 2014). Continuous hourly measurements of PNC were collected from January 1, 2004 through December 31, 2013 at the site using a butanol-based condensation particle counter (Model 3022A; TSI Inc., Shoreview, MN). Hourly values taken during each 24-h period were averaged to calculate daily mean concentrations (Chung et al., 2015; Fuller et al., 2015). We then constructed several PNC metrics during selected time periods: current day, 1-day, and 2-day lags and moving averages (MAs) of 3, 7 and 28 days. We selected time periods for evaluation based on past published observations of associations between PNC and CRP for a current-day lag up to a maximum of 28 days (Fuller et al., 2015; Hertel et al., 2010). Data on temperature was collected from a station at Logan International Airport in Boston. We averaged hourly measures for a 24 h period to calculate daily means.

2.4. Statistical analysis

The relationship between changes in ambient PNC and biomarkers was evaluated using mixed effects models with individual-specific random intercepts. Age and sex were included in the models *a priori,* given the strong association of each with the outcomes. Other covariates were included based on their strength of association with the outcome ($p\text{-value} < 0.05$) in univariate models and/or change in effect estimates of 10% or more. We considered for inclusion the following participant-level covariates: BMI, waist-hip ratio, household income, education, diabetes (self-reported yes or no), hypertension (according